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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/900,559	07/25/97	CHENG	S 226/242

EXAMINER

HM21/0323

SPIEGEL, S

ART UNIT	PAPER NUMBER
1645	4

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DATE MAILED: 03/23/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-8 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-8 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☒ The drawing(s) filed on _____ is/are objected to by the Examiner.
☒ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☒ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
☒ received.
☒ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1998-421-632/40206

DRAWINGS

The drawings are objected to for reasons on the accompanying NOTICE OF DRAFTSPERSON'S PATENT DRAWING REVIEW (PTO-948). Correction is required.

The drawings are objected to under 37 CFR 1.83(a) because they fail to show character "2" as described in the specification on page 45, line 15. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Correction is required.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. **Correction of Informalities** -- 37 CFR 1.85; 1097 O.G. 36

   New formal drawings must be filed with the changes incorporated therein. The art unit number, application number (including series code) and number of drawing sheets should be written on the reverse side of the drawings. Applicant may delay filing of the new drawings until receipt of the "Notice of Allowability" (PTO-37). If delayed, the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability" (PTO-37) to avoid extension of time fees. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a) for filing the corrected drawings (but not for payment of the issue fee). The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. **Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

   All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the three month shortened statutory period set in the "Notice of Allowability" (PTO-37). Within that three month period, two weeks should be allowed for review of the new drawings by the Office. If a correction is determined to be unacceptable by the Office, applicant must arrange to have an acceptable correction re-submitted within the original three month period to avoid the necessity of obtaining an extension of time with extension fees. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

INFORMALITIES

The disclosure is objected to because of the following informalities:

on page 46, line 18 and on page 49, line 6, "(2a)" should be --(2A)-- in accordance with Figure 1.

on page 46, line 23 and on page 50, line 9, "(5a)" should be --(5A)-- in accordance with Figure 1.

on page 47, line 10 and on page 49, line 8, "(2b)" should be --(2B)-- in accordance with Figure 1.

on page 47, line 11 and on page 49, lines 12 and 18, "(2c)" should be --(2C)-- in accordance with Figure 1.

on page 59, line 19 define "zwittergent 3-12".

all abbreviations should be fully explained the first time they are used to avoid confusion, e.g. "EDAC", "MES" and "GAS".

update the status of applications USSN 08/444,238 and 08/752,695 as appropriate.

There are no detailed descriptions of Figures 5, 6, 7, 8(a)-8(c) and 9(a)-9(c).

Appropriate correction is required.

Applicants are cautioned against introducing new matter when responding to the above objections. *N.B. The above line numbers are as indicated by applicants at the left side of the specification pages.*

TRADEMARK USAGE

The use of the trademark TWEEN 20 (pages 14, 20) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

NON-ART BASED REJECTIONS

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether "may be added" as recited in claim 1, line 6 is a positive limitation or not, i.e. are the two reagents added in any order or not.

The difference in scope between "comprising", "containing", and "having" is unclear. If there is no difference, a single term should be used to avoid confusion. If there is a difference, that difference should be clarified.

Claim 1, line 8 is vague and indefinite in reciting "introducing" as the encompassed means/method step is neither specifically (e.g. immersing a protruding sample receiving pad of a lateral flow immunochromatographic device comprising a defined structure into the post extraction mixture of step (a)) nor functionally (e.g. placing the post extraction mixture of step (a) with capillary flow communication with a first end of a lateral flow immunochromatographic device comprising a defined structure).

It is suggested that --in order-- be inserted after "steps" in claim 1, line 3 (or --sequential-- be inserted before "steps") to clarify antecedent basis problems in claim 1. For example, "said sample" in lines 11-12 apparently refers to the extracted sample, not the original sample.

Claim 1 is incomplete in failing to recite critically required reagents and/or method steps. For example, claim 1 fails to provide reagents for "forming an antigen-indicator labeling reagent complex". Critical limitations should be stated positively, not merely implied. See also step (d).

Claim 1 is confusing in reciting "antigen" and "extracted antigen" interchangeably.

It is unclear how and when the method step of claim 2 occurs within the method of claim 1. Claim 2 is similarly incomplete in failing to recite all critically required method steps and/or reagents, e.g. means for providing the positive control signal. Claim 2 is vague and indefinite in reciting a "positive control" signal as it is unclear what is being controlled for, e.g. target analyte, end-of-run, etc.

Claim 4 is confusing in reciting "further" comprise because no initial composition of the extraction reagents had been given previously.

Claim 5 is vague and indefinite in reciting a color change without reciting means for providing either said color change or said original color(s).

Claims 1-8 are vague and indefinite as to the structural design and composition of the recited "lateral flow immunochromatographic assay device".

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Both mobilizable and immobilized specific binding reagents, neutralizing reagents, control means, etc. critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The specification is only enabled for lateral flow immunochromatographic assay devices which comprise all critically required elements for the claimed immunoassay, such as mobilizable and immobilized specific binding reagents. Critical limitations must be positively recited, not merely implied.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide an adequate written description of how to provide a "pink" solution of sodium nitrite. Although page 61 of the specification refers to "the OSOM Strep A Test" and indicates that reagent 1 is "pink" and turns "light yellow" when added to reagent 2 in the test tube, the specification fails to teach or suggest either the reagents or the

reaction which produce the claimed color change. One of ordinary skill in the art would have been well aware that a solution of acetic acid is colorless and a solution of sodium nitrite is at most a very pale yellow color. Thus, it is unclear where the "pink" color came from.

ART BASED REJECTIONS

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4 and 6-8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Imrich et al. (US 5,415,994).

Imrich et al. describes a lateral flow medical diagnostic assay device with sample extraction means.

> The devices generally comprise an extraction chamber; a labelling zone having a means for specifically labelling the analyte; and a matrix defining an axial flow path in fluid communication with the extraction chamber, which matix comprises a sample receiving zone and capture zone located downstream from the sample receiving zone. The methods of detecting such analytes generally comprise inserting a swab containing the sample in the extraction chamber of the device as described above; inserting an extraction solution to the extraction chamber; observing accumulation of label in the capture zone of the device; and determining therefrom the presence or absence of the analyte in the sample. Kits comprising a device as described above and an extraction solution are also provided. (col. 2, lines 26-40)

For example, immunological detection of Group A streptococcus pretreats of a swab containing a sample of pharyngeal exudate with nitrous acid, to expose Group A specific antigens (col. 4, lines 14-19). Fluid from the extraction chamber contacts the matrix at the sample receiving zone, which zone may contain a nuetralizing agent which will neutralize the extraction solution prior to the assay (col. 5, lines 1-8). As the treated sample flows through the labelling zone, the target analyte binds labelled antibody and continues to flow into the capture zone where the presence of analyte may be determined by visual identification of label retention in the capture zone (col. 5, lines 39-52). The capture zone may include a procedural control line (col. 5, lines 53-60). Conventionally, the matrix (test strip) is contained within a solid casing (plastic housing) (col. 7, lines 11-49). The extraction solution may be contained in a single chamber vial or multi-chamber allet, which separately contains components of an unstable reaction solution. Upon mixing in the extraction chamber, the solution is activated and treats the sample. For example, nitrous acid is a

relatively unstable solution. Consequently, reagents used to generate the nitrous acid, i.e. soldium nitrite and acetic acid, are mixed immediately before initiation of the antigen extraction system (col. 8, lines 50-63). The examples (beginning at col. 10, line 10) explicitly describes detection of Group A streptococcus by means of a lateral flow assay using a nitrous acid extraction solution made of equal volumes of 1M sodium nitrite and 1M acetic acid.

Claims 3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Imrich et al. (US 5,415,994) taken in view of Bogart et al. (US 5,494,801) and Murray (US 3,957,436).

Imrich et al. has been described *supra* and differs in failing to disclose (a) vigorous mixing of the swab and extraction reagent for at least 10 seconds; and (b) an extraction solution wherein addition of 0.3 M acetic acid to a "pink" colored solution of 2M sodium nitrite produces a "light yellow" nitrous acid reagent.

Bogart et al. defines "the standard ntirous acid extraction method" as

> a mixture of 120 µl of 0.25M acetic acid and 100 µl of 2.3 M sodium nitrite (previously dried into the extraction tube) is used to generate nitrous acid. The acetic acid is found to effectively extract antigen in the range of 0.1M to 1.0M. Antigen is extracted from the organism for 5 minutes, although a range from instantaneous to 30 minutes is acceptable. The solution is neutralized using 120 µl of a buffer containing 1.5 M MOPSO, pH 7.3, 0.2% TWEEN 20™ detergent, 15% bovine serum, 0.5% PROCLIN300™ preservative, AND 20 mM EGTA. A final pH range of 7.0 to 7.5 is desired. (¶ bridging cols. 10-11)

Murray teaches coloring assay reagents with inert colorants such that as each step in a procedure such as an immunoassay is completed, a resultant color change indicates which steps in the procedure have been accomplished.

It would have been obvious to one of ordinary skill in the art to optimize the experimental parameters and reagents of the method of Imrich et al. by selecting such conventional components for generating nitrous acid and times of extraction as described by Bogart et al. Where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill. *In re Aller*, 220 F.2d 454, 105 USPQ 233 (CCPA 1955). Secondly, it would have been further obvious to use inert colorants in one or more reagents of the assay of Imrich et al. which change color upon completion of the reaction in which said one or more reagents are used as a quality control measure to conclusively indicate that method step or reaction has been accomplished as suggested by Murray.

CLOSING

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Fischetti et al. (US 5,604,109) detects Group A streptococcal antigens using a lysin extraction step followed by immunochemical assay.

Huang et al. (US 5,712,172) describes an immunochromatographic test device.

Eisinger et al. (US 4,943,522) describes a lateral flow, non-bibulous membrane assay method and device therefore. Example 7 illustrates an assay for Group A streptococcus.

Friesen et al. (US 4,861,711) describes conventional immunochromatographic test devices.

The specification referenced a number of commercially available tests kits for determination of Group A Streptococcus. If readily available to applicants, the examiner would appreciated a copy of the product inserts from these kits.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carol A. Spiegel whose telephone number is (703) 308-3986.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Carol A. Spiegel
March 9, 1998

Carol A. Spiegel
CAROL A. SPIEGEL
PRIMARY EXAMINER
GROUP ~~1800~~ 1600